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PREFACE

How and Why? The lab *versus* the field

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The central topics of this journal, sleep and biological rhythms, are currently among the most challenging and promising realms of science. The journal *Science* celebrated its 125th anniversary in 2005 by asking: What don't we know? It selected 125 important questions which scientists may well answer in the first quarter of the 21st century. Three of these directly refer to our area: What synchronizes an organism's circadian clocks? Why do we sleep? Why do we dream?

"Why do we sleep?" is indeed the most intriguing question in behavioral biology. We know why we eat, why we drink, why we mate, why we walk, why we wash and groom. Sleep is the only widespread behavior whose function we do not know. Humans spend one third of their lives doing it. We know that we need sleep and that we feel refreshed after it, but we don't know why that is. "Why?" is shorthand for "what are the positive effects on individual fitness that keep the behavior in the genomic program of animals". Fitness, in the Darwinian sense, is the expected rate of gene propagation by the individual. In biology, every phenomenon can be addressed with a "why" question and a "how" question. "Why" refers to the evolutionary consequences, and "how" to the physiological mechanisms. Sleep and biological rhythms are behavioral phenomena that are studied in laboratories worldwide. The scientific interest is broad and increasing. Society is beginning to appreciate the importance of deeper insight into both the causes and consequences of these phenomena: into "how" and "why".

The "how" question is being answered at a rapid pace in the lab. It is astonishing how deep the research has penetrated into the mechanisms underlying these behaviors. In several regards, chronobiology is way ahead of other realms of neuroscience. The transplantation of neuronal tissue containing circadian pacemakers from one animal to another without loss of function is a unique achievement. The unraveling of the circadian machinery at the molecular level has gone further than in the mechanisms of any other behavior.

Answering the "why" question demands an understanding of the behavior in nature. Yet attempts to understand the contribution of sleep and rhythms to survival and reproduction remain truly limited. Data obtained in the laboratory are of little help. Indeed, they sometimes offer awkward misguidance in our basic understanding. In sleep research, comparative analysis has relied solely on data from captivity (either the lab or the zoo). The three-toed sloth has been the champion sleeper for decades, with a recorded daily sleep duration of 16 h. Rattenborg *et al.* recently equipped sloths in Panama with tiny EEG loggers and found that they sleep no more than 9.6 h per day in the wild.[1] Other animals will also turn out to sleep less in nature than in the zoo. The lab and the zoo are boring luxury prisons, where animals do not have to work for their food and easily survive with less wakefulness than they need in nature. Such effects need not compromise our understanding of physiological mechanisms, but they lead to dramatic misconceptions in the interpretation of function.

Mice and hamsters are prime targets of circadian rhythms research. They owe this privilege to their precise expression of endogenously generated rhythms of nocturnal activity and diurnal rest. Researchers worldwide assume that this pattern reflects their behavior in nature. This is wrong: recent studies show that the activity in both species in the field is to a large extent diurnal rather than nocturnal. Nocturnality and precision of timing are the consequence of the special circumstances of a lab cage, with permanent *ad libitum* food and no more exercise than a running wheel.

This insight not only affects our understanding of function, but also of physiological mechanism. The standard approach is that SCN (suprachiasmatic nucleus) itself controls activity. In the natural situation activity rhythms have only a loose phase relationship to the pacemaker. This loose control becomes evident under special conditions, such as caloric restriction, in mice and rats that have to work for their food, or under the influence of methamphetamine. The use made of endogenous clocks is probably subtle and adaptive. Circadian pacemakers may well act as internal consultable clocks telling the time of day, rather than as control systems dictating preprogrammed behavior.

The one species that largely escapes the flaws inherent in the lab condition is the human itself. Human studies are necessarily often performed in our natural environment or a close approximation of it. This may be why they have contributed so much to the analysis of sleep and rhythms. Humans have many advantages as a model species, apart from the fact of more easily available funding. Humans have the potential to yield vast data sets. The huge data base on human timing assembled in the Munich Chronotype Questionnaire (MCTQ)[2] is unprecedented in animals. Our civil administration keeps track of the genealogy of virtually the whole world population. This could provide the demographic data needed for true Darwinian fitness analyses, even if this potential remains underexploited. Our skulls, with virtually no subcutaneous musculature, are ideal for sleep EEG: no need to drill holes. Primary insights, such as the REM–nREM dichotomy and the homeostasis of sleep, stem from research on humans, not animals. Even in isolation units, our sleep is close to our natural behavior. In such studies, humans were the first species to show internal desynchronization – the uncoupling of behavior from the circadian pacemaker. Unlike animals, humans can tell whether and what they dream. Human studies will in the future contribute greatly to answering the "why" questions.

In animal research, much will depend on increasing the sophistication of field studies. The use of advanced and miniaturized data-logging systems is rapidly spreading. They can collect behavioral and physiological data from animals in unrestrained natural conditions on a scale unprecedented in classical behavioral studies. Accelerometry sensors now allow continuous records of specific individual behavior in the wild.[3] Logging heart rate yields precise estimates of energy metabolism. Logging EEGs, as applied to the sloths, brings measurement of natural sleep patterns within reach.

We may be in for surprises. Recent studies show sperm whales hanging vertically motionless in the water, elephant seals resting in the safety of deep water in the early morning,[4] and large ungulates with nocturnal hypometabolism in winter. For a real answer to the "why" questions, we need to understand the variation of behavior in nature, variations between species, variations between individuals, and variations between environmental situations. The lab is the key to understanding the mechanism, while the field is the key to understanding function. We need both.

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